REMARKS

Applicants have amended Claims 1-4, and added new claims 5-8. Enabling support for the amendments and for the new claims can be found in the application as filed, and therefore no new matter is contained in the amendment. Reconsideration of the present application and allowance of resulting Claims 1 through 8 is respectfully requested in view of the amendment and the following remarks.

I. Claim Rejections Under 35 U.S.C. § 112, first paragraph

The Office Action rejected Claims 1-4 under 35 U.S.C. § 112, first paragraph for failing to comply with the written description requirement by the addition of new matter. The Office Action stated that the sections of the specification cited by Applicants in their response to the previous Office Action did not contain support for the new limitation that the DNA vector be "non-viral."

Applicants have amended Claims 1-4 to recite a "plasmid vector construct" rather than a "non-viral vector construct." By amendment of these claims, applicants do agree with the Examiner's assertion but only to advance the prosecution of the present application. Applicants reserve the right to prosecute the original subject matter in these claims in one or more continuation or divisional applications.

Applicants respectfully submit that the specification as filed provides support for the addition of the term "plasmid" to the claims. In particular, Applicants submit that the specification contains such support on page 7, lines 3-4. For example, the vector described under the Methods (DNA Constructs) section describes a plasmid DNA vector construct that was created by subcloning the EGFP coding sequence from the pEGFP plasmid vector into the pIRES plasmid vector. (See page 12, line 25 to page 13, line 13.) This plasmid vector construct places the neomycin resistance gene and the EGFP gene sequences under the control of a single promoter, the human cytomegalovirus (CMV) promoter.

As sufficient support for the term "plasmid" is present in the specification as filed, Applicants respectfully request that the rejections under 35 U.S.C. § 112, first paragraph be withdrawn.

II. Claim Rejections Under 35 U.S.C. § 103

The Office Action rejected Claims 1, 2, 3, and 4 under 35 U.S.C. § 103(a) as being unpatentable over the Rees et al. reference (Biotechniques (1996) 20:102-110) in view of the Cheng et al. reference (Gene Therapy (1997) 4:1013-1022). The Office Action stated that the Rees et al. reference teaches a non-viral bicistronic DNA vector construct comprising an IRES, and a selection marker, and that the vector could be used to obtain stably transfected cells or cell lines. The Office Action further stated that the Rees et al. reference does not teach placement of the GFP into the vector nor placement into stem cells. The Office Action also stated that Cheng et al. teach a DNA vector construct comprising an IRES, a selection marker, and a green fluorescent protein; stably transfected cells with the vector; and stable transfection of stem cells. Applicants respectfully submit that Claims 1-4, as amended, are not obvious over the Rees et al. reference, in view of the Cheng et al. reference.

"Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination." *ACS Hospital Systems, Inc. v. Montefiore Hospital*, 732 F.2d 1572, 1577 (Fed. Cir. 1984). Applicants respectfully submit that the prior art does not provide the necessary teaching, suggestion, or incentive to combine the teachings of the cited references to arrive at the present invention. The present invention relates to a plasmid vector comprising a selection marker and a green fluorescent protein gene that are transcribed as a single mRNA transcript. The present application discloses that such a non-viral vector is useful to efficiently create stably transfected cells which comprise the vector and that the dicistronic expression of the selection marker and a green fluorescent protein genes of the present invention allows for the simplified selection and maintenance of positive transfectants. The present invention also discloses that the use of this vector allows one to effectively monitor cell motility, and in particular, stem cell and

tumor cell migration. The genes on the non-viral DNA vector construct of the present invention are stably expressed in the transfected cells.

The Rees et al. reference suggests the use of non-viral vectors comprising an IRES and a selection marker to obtain stably transfected cells or cell lines. Rees et al. describe the use of a vector with a bicistronic expression system to allow a practitioner to be sure that his protein of interest is being expressed in a transfected cell in order that he may study his protein of interest in the transfected cell. The examples of potential applications given by Rees et al. are 1) to identify stable clones which express high levels of recombinant protein for functional analysis and 2) particularly to produce a serotonin receptor in order to screen potential ligands (column 3, page 109). Rees et al. designed their vector with the production of large quantities of recombinant proteins in mind. However, this reference does not suggest that the use of a selection marker and a green fluorescent protein as a dicistronic transcript would allow a means for the efficient selection and monitoring of transfectants. There is no suggestion in Rees et al. that the bicistronic expression system would be useful for the efficient expression of two selection markers or for the efficient monitoring of the motility of transfected cells. There is no suggestion in Rees et al. to using the plasmid to create constructs encoding proteins for any reason other than protein production, as opposed to mere protein expression. Moreover, Rees et al. does not make any reference to the desirability of being able to express a protein that confers visibility to cells.

Cheng et al. describe the transduction of hematopoietic stem cells with a retroviral vector comprising the EGFP gene in order to develop a reporter system for optimum retrovirus-mediated gene transfer into human primitive hematopoietic progenitors. The retroviral vectors were chosen as a "primary choice as a vehicle for gene delivery since they are capable of integrating into cellular chromosomes, resulting in stable transmission to every progeny cell derived from transduced [hematopoietic stem and progenitor cells]." (*See* Cheng et al., page 1013, column 1.) Therefore, the Cheng et al. reference can be said to teach away from the presently claimed invention using non-viral DNA vector construct. There are many disadvantages of using a retroviral vector system as has been discussed previously. For example, transduction procedure is lengthy and cumbersome; the integration of the retroviral vector DNA

into the host cell DNA is random; non-native DNA sequences may be excised from the chromosomal DNA at a high rate; and retroviral genes may elicit an immune response in a host organism.

"The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." MPEP §2143.01, *citing In re Mills*, 916 F.2d 680 (Fed. Cir. 1990). Despite the longfelt need for improved systems for transfecting cells for monitoring cellular motility, there has been no suggestion of achieving the same with the advantages of the presently claimed compositions. Applicants respectfully submit that the Office Action applies hindsight analysis to consider the combination of the cited references to render the claimed invention obvious, and that one of ordinary skill in the art at the time of this invention would not have been prompted to combine the teachings of these references to arrive at the present invention. Accordingly, Applicants respectfully request that the rejections of Claims 1-4 under § 103 be withdrawn.

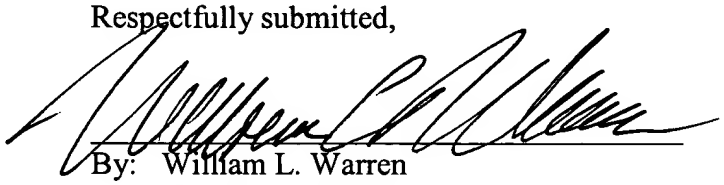
III. Concluding Remarks

For at least the foregoing reasons, Applicants respectfully request reconsideration and removal of the rejections and allowance of Claims 1-8. The foregoing is submitted as a full and complete Response to the Office Action mailed October 15, 2004.

A petition for a one month extension of time, as well as fees in the amount of $60.00, are being submitted concurrently herewith. No additional fees are believed due; however, the Commissioner is hereby authorized to charge any additional fees that may be required, or credit any overpayment to Deposit Account No. 19-5029.

This Response places all claims in the present application in condition for allowance, and such action is courteously solicited. The Examiner is invited and encouraged to contact the undersigned attorney of record if such contact will facilitate an efficient examination and allowance of the application.

Respectfully submitted,



By: William L. Warren
Reg. No. 36,714

Date: February 15, 2004

SUTHERLAND ASBILL & BRENNAN LLP
999 Peachtree Street, N.E.
Atlanta, GA 30309
Tel No. (404) 853-8081
Fax No. (853) 853-8806
SAB Docket: 18377-0034